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Commentary

The pons and human affective processing – Implications for Parkinson's disease



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Affective processing determines how we react to stimuli, interact with the surroundings and perceive the world. It shapes our behaviour. In their article in this issue of *EBioMedicine*, Lee et al. (Lee et al., 2015) shed light on the involvement of the pons in affective processing in healthy volunteers.

The authors report the findings of experiments where they showed images to adult women. The images consisted of visual stimuli containing a positive, neutral or negative affective charge. They conducted blood-oxygen-level dependent (BOLD) contrast functional magnetic resonance imaging (fMRI) to determine brain metabolism during the visualising and subsequent emotional processes. Specifically, they analysed task-based BOLD signals, tested small-world connectivity and examined resting-state functional and diffusion tensor imaging (DTI) structural connectivity.

They discovered that showing positive visual stimuli results in activation of a pontine region, possibly the caudal raphe nuclei. A significant functional connectivity was found between the pons and cortico-sub-cortical structures involved in affective processing, encompassing the caudate nucleus, thalamus, hippocampus, amygdala, as well as the cingulate, insular and frontal cortices. The authors conclude that their findings indicate that the pons forms a network with “cortico-limbic-striatal” systems to mediate one's affective state after seeing emotionally-charged images.

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Whereas Lee et al.'s study was conducted in a sample of subjects without prior neuro-psychiatric history, as pointed out by the authors, their results suggest that the pons might play a role in affective/mood disorders. Depressive and related disorders are a category of mood disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). It is noteworthy that depression is encountered in several neuro-degenerative diseases, such as Parkinson's disease (PD). What do the findings of Lee et al. might mean for PD patients?

In PD, the pons degenerates, encompassing serotonin (5-HT)-producing raphe nuclei (Halliday et al., 1990). The role of 5-HT in mood and affect has been well-documented (Berger et al., 2009). As many as 30–40% of PD patients are afflicted by depressive symptoms (Aarsland et al., 2009). Tallying this to the results of Lee et al., it becomes plausible that dysfunctional pontine structures might play a role in mood disorders in PD.

Several in vivo imaging studies have examined the raphe 5-HT transporter in PD, via either positron emission tomography (PET) or single-photon emission computed tomography (SPECT) modalities. However, as these PET and SPECT studies were designed to study the 5-HT transporter function, they would, at most, provide only indirect assessment of the pons per se. Moreover, several of these were conducted in non-depressed patients (Guttman et al., 2007; Politis et al., 2010a) or focussed on other regions of interest, e.g. the midbrain (Haapaniemi et al., 2001; Berding et al., 2003).

Two studies are worth discussing here, as they assessed the 5-HT transporter binding in the caudal raphe nuclei, which are located in the pons. In a recent SPECT study encompassing 345 early, drug-naïve male and female PD patients, there was no correlation between raphe (rostral and caudal) 5-HT transporter binding and depression (Qamhawi et al., 2015). In contrast, in a PET study encompassing PD patients with and without depression and healthy controls, caudal raphe nuclei 5-HT transporter binding was lower in non-depressed PD patients when compared to depressed PD patients and healthy controls, while no difference was encountered between depressed PD patients and controls (Politis et al., 2010b). It should be noted that the PD patients from this last study were more advanced than those from the first study and were not drug-naïve, thus making the PD populations from the two studies difficult to compare. The fate of 5-HT transporter located in the caudal raphe nuclei therefore appears unclear in PD and possibly varies according to disease progression and medication intake. Nevertheless, the second study suggests that 5-HT transporter binding is higher in depressed PD

patients compared to depressed patients; how does that relate to the increased metabolic activity found by Lee et al. in the pons in their study needs to be further investigated.

In summary, Lee et al.'s results point out that the pons might be involved in affective processing of visual stimuli. Their study refines the understanding of affective processing and has implications to better understand the networks underlying affective processing in the physiological state. It also provides a new neuro-anatomical substrate to investigate in neuro-degenerative conditions where there are affective/mood disorders such as PD.

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